REMARKS

Upon further consideration of this case, it was recognized that claim 1 should be restructured in non-Jepsom form to more clearly set forth the invention for which patent protection is sought. New claim 21 is claim 1 which has been so restructured. While the format is different, the scope of the claim is the same as previously. New claims 22-33 correspond to prior claims 2-13.

The Office Action of August 28, 2000 rejected claims as being indefinite by asserting that the acronym SERM was being used "inappropriately." SERM is an acronym for Selective Estrogen Receptor Modulator and the claims used (and still use) the full name rather than the acronym. Both the full name and the acronym are terms of art and are being so used in their art understood sense in this application. Why the Office Action asserted that the terminology was being used "inappropriately" is not understood and is not adequately explained in the Action. Therefore, the rejection is respectively traversed.

More particularly, the Office Action makes reference to Goldstein on page 1480, as teaching that SERMs have both agonist and antagonist effects and states that such teaching "renders the instant rebuttal argument unconvincing". That statement is not understood. Applicants previously pointed out that Goldstein stated that the SERMs mimic the effects of estrogen in some tissues and act as antagonist in others. In fact, that disclosure is in the very sentence preceding the disclosure to which the Action refers. Both statements are correct. SERMs are both agonistic and antagonistic but the target tissue determines the expression of these activities. For example, SERMs are agonistic in bone but antagonistic in the hypothalamus. Regardless, the terminology has a well-known art recognized meaning and that the terminology was being used in accordance with that well known art recognized meaning in the claims. Additional references to show this fact are enclosed.

The statements in the last amendment were with reference to the fact that an inaccurate interpretation of the terminology had been used in the previous Office Actions and essentially deemed any compound which modulated estrogen receptor activity in any fashion was a SERM.

The applicant's point was that such a definition was not the accepted definition of SERM in the art.

In light of these considerations, it is respectfully submitted that the term SERM is being used in its clear and definite art recognized definition. In the event that the Examiner still believes that the terminology is being used "inappropriately," it is respectfully requested that a more detailed explanation of the basis of this rejection be set forth so that the applicant can make an appropriate response.

This application is a Division of an original filing and is particularly concerned with the joint use of a SERM and an agent which exhibits progestogenic activity. The two agents act jointly into provide the desired contraception. As pointed out on the opening pages of the application, estrogen is known to induce bleeding as a side effect of their use and SERMs (also known as anti-estrogens) are known to actually exaggerate the estrogen side effects which their use sought to avoid. It is also known in the art that progestogenic agents have side effects such as hot flashes. In the present invention, the two agents act together providing a contraceptive effect as well as preventing the hypothalamus and pituitary from operating in a deranged manner so that each agent modulates the side effects of the other.

Rejections in the Office Action of August 28, 2000 under Sections 102 or 103 were advanced over Garfield against claims 1, 3-5 and 7-13. Claims 2 and 6 were indicated to be allowable if the rejection under Section 112 was overcome.

The Garfield reference does not anticipate or render any of the instant claims obvious. The patent relates to ovulation control by regulating nitrogen oxide levels. Ovulation control includes both contraception and stimulation of ovulation. The reference does teach that oral contraception can be achieved by the use of various agents including progestins. To prevent ovulation (contraception), Garfield teaches combining the use of the progestin with a nitric oxide synthesis inhibitor for the purpose of lowering the nitrogen oxide level. To achieve the opposite effect, namely stimulation of ovulation, Garfield teaches combining a nitric oxide source with other materials including, specifically, clomiphene. Clomiphene is the only SERM disclosed in this reference and it is explicitly taught at column 3, lines 12-14, to be an agent "which stimulates ovulation". In the hypothalamus, SERMs are antagonistic, resulting in blocking the

action of estrogen which increases the secretion of the gonadotropin releasing hormone, which in turn increases LH and FSH secretion from the pituitary, which in turn stimulates follicle growth and ovulation. Therefore, the use of a SERM, and particularly clomiphene, in a contraceptive method is clearly contraindicated. Garfield explicitly suggests that the clomiphene would counteract the desired contraceptive effect by stimulating ovulation. Garfield neither teaches administering a combination of a progestogenic compound and a SERM and the relevant teachings are that a SERM would not be used in a contraceptive method. Clearly, therefore, the claimed invention is unobvious.

The present invention is based on the discovery that the SERM and progestogenic material act in tandem, each modulating the active of the other in the hypothalamus-pituitary axis and each modulating the side effects of the other. There is no teaching or suggestion of the invention in Garfield.

In light of all of the foregoing, the early further examination and allowance of this application is respectfully solicited.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on February 28, 2001

Edward A. Meilman
Name of applicant, assignee or Registered Representative

Signature

February 28, 2001
Date of Signature

Respectfully submitted,

Edward A. Meilman
Registration No.: 24,735
OSTROLENK, FABER, GERB & SOFFEN, LLP
1180 Avenue of the Americas
New York, New York 10036-8403
Telephone: (212) 382-0700

APPENDIX A

"CLEAN" VERSION OF EACH PARAGRAPH/SECTION/CLAIM
37 C.F.R. § 1.121(b)(ii) AND (c)(i)

CLAIMS (with indication of amended or new):

New: 21. A method of achieving contraception in a premenopausal female by administering to the female a contraception effective amount of a combination of a Selective Estrogen Receptor Modulator and an agent which exhibits progestogenic activity, wherein the amount of the agent which exhibits progestogenic activity is effective to modulate the side effects of the Selective Estrogen Receptor Modulator.

New: 22. The method of claim 21 wherein the Selective Estrogen Receptor Modulator is clomiphene.

New: 23. The method of claim 21 wherein the Selective Estrogen Receptor Modulator is a benzothiophene.

New: 24. The method of claim 21 wherein the agent which exhibits progestogenic activity is an antiprogestin.

New: 25. The method of claim 24 wherein the antiprogestin is a progesterone receptor antagonist.

New: 26. The method of claim 25 wherein the Selective Estrogen Receptor Modulator is clomiphene.

New: 27. The method of claim 25 wherein the Selective Estrogen Receptor Modulator is a benzothiophene.

New: 28. The method of claim 24 wherein the amount of antiprogestin is that sufficient to maintain the blood estrogen concentration in the range of about 25 to 125 pg/ml.

New: 29. The method of claim 28 wherein the amount of antiprogestin is that sufficient to maintain the blood estrogen concentration in the range of about 60 to 90 pg/ml.

New: 30. The method of claim 21 wherein the agent which exhibits progestogenic activity expresses both androgenic and progestogenic activity.

New: 31. The method of claim 30 wherein the agent which exhibits progestogenic activity comprises the combination of an androgen and a progestin.

New: 32. The method of claim 30 wherein the agent which exhibits progestogenic activity is a single material which expresses both activities.

New: 33. The method of claim 32 wherein the agent which exhibits progestogenic activity is danazol or levonorgestrel.